



RAB3GAP1 gene

RAB3 GTPase activating protein catalytic subunit 1

Normal Function

The *RAB3GAP1* gene provides instructions for making a protein that helps regulate the activity of specialized proteins called GTPases, which control a variety of functions in cells. To perform its function, the RAB3GAP1 protein interacts with another protein called RAB3GAP2 (produced from the *RAB3GAP2* gene) to form the RAB3GAP complex.

Often referred to as molecular switches, GTPases can be turned on and off. They are turned on (active) when they are attached (bound) to a molecule called GTP and are turned off (inactive) when they are bound to another molecule called GDP. The RAB3GAP complex turns on a GTPase known as RAB18 by exchanging GTP for the attached GDP. When active, RAB18 is involved in a process called vesicle trafficking, which moves proteins and other molecules within cells in sac-like structures called vesicles. RAB18 regulates the movement of substances between compartments in cells and the storage and release of fats (lipids) by structures called lipid droplets. The protein also appears to play a role in a process called autophagy, which helps clear unneeded materials from cells. RAB18 is important for the organization of a cell structure called the endoplasmic reticulum, which is involved in protein processing and transport.

The RAB3GAP complex is also thought to inactivate another GTPase known as RAB3 by stimulating a reaction that turns the attached GTP into GDP. RAB3 plays a role in the release of hormones and brain chemicals (neurotransmitters) from cells.

Health Conditions Related to Genetic Changes

RAB18 deficiency

More than 60 *RAB3GAP1* gene mutations have been found to cause RAB18 deficiency, resulting in conditions that affect the eyes, brain, and reproductive system. The two conditions caused by this deficiency are Warburg micro syndrome at the severe end of the spectrum and Martsolf syndrome at the mild end. *RAB3GAP1* gene mutations are the most common cause of Warburg micro syndrome and are rare in Martsolf syndrome.

Warburg micro syndrome is caused by *RAB3GAP1* gene mutations that prevent the production of any RAB3GAP1 protein or completely eliminate its function. Martsolf syndrome occurs when a small amount of functional RAB3GAP1 protein is produced from the mutated gene. Reduction or loss of this protein likely impairs the formation or function of the RAB3GAP complex, leading to a shortage (deficiency) of RAB18

activity. It is unclear why the loss of RAB18 function leads to eye problems, brain abnormalities, and other features of these two conditions.

Because Warburg micro syndrome and Martsolf syndrome can be caused by mutations in other genes that disrupt normal RAB18 activity, loss of control of this GTPase is thought to underlie the conditions. It is unclear if impaired regulation of RAB3 activity contributes to the features of Warburg micro syndrome or Martsolf syndrome.

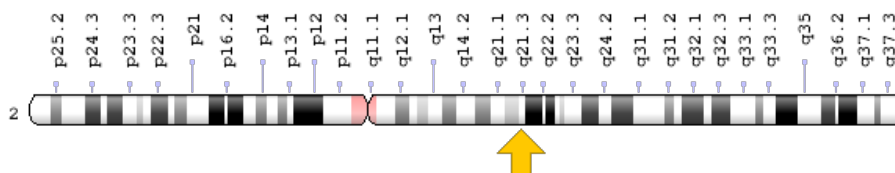
Coloboma

Keratoconus

Chromosomal Location

Cytogenetic Location: 2q21.3, which is the long (q) arm of chromosome 2 at position 21.3

Molecular Location: base pairs 135,052,281 to 135,176,667 on chromosome 2 (Homo sapiens Updated Annotation Release 109.20200522, GRCh38.p13) (NCBI)



Credit: Genome Decoration Page/NCBI

Other Names for This Gene

- KIAA0066
- P130
- rab3-GAP p130
- RAB3 GTPase-activating protein 130 kDa subunit
- rab3 GTPase-activating protein catalytic subunit isoform 1
- rab3 GTPase-activating protein catalytic subunit isoform 2
- RAB3 GTPase activating protein subunit 1 (catalytic)
- RAB3GAP
- RAB3GAP130
- WARBM1

Additional Information & Resources

Educational Resources

- Basic Neurochemistry: Molecular, Cellular and Medical Aspects (6th edition, 1999):
Small G proteins
<https://www.ncbi.nlm.nih.gov/books/NBK28084/>

Scientific Articles on PubMed

- PubMed
<https://www.ncbi.nlm.nih.gov/pubmed?term=%28%28RAB3GAP1%5BTIAB%5D%29+OR+%28RAB3+GTPase+activating+protein+catalytic+subunit+1%5BTIAB%5D%29%29+AND+%28%28Genes%5BMH%5D%29+OR+%28Genetic+Phenomena%5BMH%5D%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+1800+days%22%5Bdp%5D>

Catalog of Genes and Diseases from OMIM

- RAB3 GTPase-ACTIVATING PROTEIN, CATALYTIC SUBUNIT
<http://omim.org/entry/602536>

Research Resources

- Atlas of Genetics and Cytogenetics in Oncology and Haematology
http://atlasgeneticsoncology.org/Genes/GC_RAB3GAP1.html
- ClinVar
<https://www.ncbi.nlm.nih.gov/clinvar?term=RAB3GAP1%5Bgene%5D>
- HGNC Gene Symbol Report
https://www.genenames.org/data/gene-symbol-report/#!/hgnc_id/HGNC:17063
- Monarch Initiative
<https://monarchinitiative.org/gene/NCBIGene:22930>
- NCBI Gene
<https://www.ncbi.nlm.nih.gov/gene/22930>
- UniProt
<https://www.uniprot.org/uniprot/Q15042>

Sources for This Summary

- Aligianis IA, Johnson CA, Gissen P, Chen D, Hampshire D, Hoffmann K, Maina EN, Morgan NV, Tee L, Morton J, Ainsworth JR, Horn D, Rosser E, Cole TR, Stolte-Dijkstra I, Fieggen K, Clayton-Smith J, Mégarbané A, Shield JP, Newbury-Ecob R, Dobyns WB, Graham JM Jr, Kjaer KW, Warburg M, Bond J, Trembath RC, Harris LW, Takai Y, Mundlos S, Tannahill D, Woods CG, Maher ER. Mutations of the catalytic subunit of RAB3GAP cause Warburg Micro syndrome. *Nat Genet.* 2005 Mar;37(3):221-3.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/15696165>
- Feldmann A, Bekbulat F, Huesmann H, Ulbrich S, Tatzelt J, Behl C, Kern A. The RAB GTPase RAB18 modulates macroautophagy and proteostasis. *Biochem Biophys Res Commun.* 2017 May 6; 486(3):738-743. doi: 10.1016/j.bbrc.2017.03.112. Epub 2017 Mar 22.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/28342870>
- Gerondopoulos A, Bastos RN, Yoshimura S, Anderson R, Carpanini S, Aligianis I, Handley MT, Barr FA. Rab18 and a Rab18 GEF complex are required for normal ER structure. *J Cell Biol.* 2014 Jun 9; 205(5):707-20. doi: 10.1083/jcb.201403026. Epub 2014 Jun 2.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/24891604>
Free article on PubMed Central: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4050724/>
- Handley MT, Carpanini SM, Mali GR, Sidjanin DJ, Aligianis IA, Jackson IJ, FitzPatrick DR. Warburg Micro syndrome is caused by RAB18 deficiency or dysregulation. *Open Biol.* 2015 Jun;5(6):150047. doi: 10.1098/rsob.150047.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/26063829>
Free article on PubMed Central: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4632505/>
- OMIM: RAB3 GTPase-ACTIVATING PROTEIN, CATALYTIC SUBUNIT
<http://omim.org/entry/602536>
- Sakane A, Manabe S, Ishizaki H, Tanaka-Okamoto M, Kiyokage E, Toida K, Yoshida T, Miyoshi J, Kamiya H, Takai Y, Sasaki T. Rab3 GTPase-activating protein regulates synaptic transmission and plasticity through the inactivation of Rab3. *Proc Natl Acad Sci U S A.* 2006 Jun 27;103(26): 10029-34. Epub 2006 Jun 16.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/16782817>
Free article on PubMed Central: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1502500/>

Reprinted from Genetics Home Reference:
<https://ghr.nlm.nih.gov/gene/RAB3GAP1>

Reviewed: April 2018
Published: June 23, 2020

Lister Hill National Center for Biomedical Communications
U.S. National Library of Medicine
National Institutes of Health
Department of Health & Human Services